PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

RECEIVED
28 FEB. 2000
HØIBERG

HØIBERG APS
Nørre Farimagsgade 37
DK-1364 Copenhagen K
DANEMARK

Date of mailing (day/month/year) 17 February 2000 (17.02.00)	
Applicant's or agent's file reference P 343 PC00	**IMPORTANT NOTIFICATION**
International application No. PCT/DK99/00605	International filing date (day/month/year) 05 November 1999 (05.11.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 05 November 1998 (05.11.98)
Applicant CHEMOMETEC A/S et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
05 Nove 1998 (05.11.98)	PA 1998 01433	DK	20 Janu 2000 (20.01.00)
11 Nove 1998 (11.11.98)	PA 1998 01469	DK	20 Janu 2000 (20.01.00)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Taïeb Akremi

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 July 2000 (03.07.00)	
International application No. PCT/DK99/00605	**Applicant's or agent's file reference** P 343 PC00
International filing date (day/month/year) 05 November 1999 (05.11.99)	**Priority date** (day/month/year) 05 November 1998 (05.11.98)
Applicant ARNVIDARSON, Börkur	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

31 May 2000 (31.05.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Manu Berrod
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

DK9900605

The International Bureau of WIPO
34, chemin des Colombettes
CH-1211 Geneva 20
Switzerland

COPY

1. May 2001 by fax 41 22 740 14 35
confirmation by mail

PCT Application No. PCT/DK99/00605
Applicant: ChemoMetec A/S
Our ref: P 343 PC00

Dear Sirs,

With reference to Rule 92bis1, please record the following changes in respect of the above identified application:

Please enter the following person being a Danish national as inventor in respect of all designated states and applicant for the United States :

Martin Glensbjerg
Næsbyholmvej 2, 4. tv
DK-2700 Brønshøj
Denmark

Please delete the following person as inventor and applicant:

Börkur Arnvidarson (IS)
Rørmosen 204
DK-2900 Nivå
Denmark

Please confirm by return facsimile that these changes have been recorded prior to expiration of the time limit in Article 39(1)(a).

Yours sincerely,
HØIBERG ApS

Jens Viktor Nørgaard

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
P 343 PC00		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/DK 99/ 00605	05/11/1999	05/11/1998
Applicant		
CHEMOMETEC A/S et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 02 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 3

   [ ] as suggested by the applicant.

   [X] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 99/00605

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: G01N 15/14
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 9850777 A1 (CHEMOMETEC A/S), 12 November 1998 (12.11.98), abstract	1-128
	--	
A	US 5457526 A (TOKIHIRO KOSAKA), 10 October 1995 (10.10.95), abstract	1-128
	--	
A	WO 9707390 A1 (FOSS ELECTRIC A/S), 27 February 1997 (27.02.97), abstract	1-128
	--	
A	WO 9734139 A1 (HAMANN, OLIVER ET AL), 18 Sept 1997 (18.09.97), abstract	1-128
	--	

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search
22 February 2000

Date of mailing of the international search report
20.03.00

Name and mailing address of the International Searching Authority
European Patent Office P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel(+31-70)340-2040, Tx 31 651 epo nl,
Fax(+31-70)340-3016

Authorized officer
MOA EMLING/ELY
Telephone No.

SA 256899

INTERNATIONAL SEARCH REPORT
Information on patent family members

02/12/99

International application No.
PCT/DK 99/00605

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9850777 A1	12/11/98	AU 7205798 A	27/11/98
		AU 7372298 A	27/11/98
		WO 9850577 A	12/11/98
US 5457526 A	10/10/95	JP 6058928 A	04/03/94
WO 9707390 A1	27/02/97	AU 6732796 A	12/03/97
		EP 0846259 A	10/06/98
		US 5978435 A	02/11/99
WO 9734139 A1	18/09/97	AU 2319197 A	01/10/97
		US 5748311 A	05/05/98

[redacted]ENT COOPERATION TRE[redacted]

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P 343 PC00		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK99/00605	05/11/1999	05/11/1998
International Patent Classification (IPC) or national classification and IPC G01N1/00		
Applicant CHEMOMETEC A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 15 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
31/05/2000	16. 01. 01
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Loades, M Telephone No. +49 89 2399 2184

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK99/00605

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-34	as originally filed			

Claims, No.:

1-96	as received on	06/11/2000	with letter of	03/11/2000
97-129	as received on	30/11/2000	with letter of	28/11/2000

Drawings, sheets:

1/6-6/6	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-96,108-129
	No:	Claims	97-107
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-129
Industrial applicability (IA)	Yes:	Claims	1-129
	No:	Claims	

2. Citations and explanations
   see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

   see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the

claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents, cited in the search report, are referred to in this report:
   D1: see Item VI
   D2: US 5 457 526 A (TOKIHIRO KOSAKA) 10 October 1995
   D3: WO 97 07390 A1 (FOSS ELECTRIC A/S) 27 February 1997
   D4: WO 97 34139 A1 (HAMANN, OLIVER ET AL) 18 September 1997
   The following documents, not cited in the search report, are also referred to in this report:
   (cited in the first written opinion):
   D5: see Item VI
   D6: EP-A-0679889
   D7: EP-A-0392851
   (cited in a telephone conversation on 24.10.00):
   D8: US-A-4338024
   D9: US-A-5517870
   D10: US-A-5469251
   (cited in a telephone conversation on 17.11.00):
   D11: US-A-5371020
   D12: US-A-5571479
   D13: US-A-4560269
   (cited in a telephone conversation on 22.11.00):
   D14: US-A-4088448
   D15: US-A-5674457

2. Review of the prior art documents:

(D1 and D5 were published before the priority date of the application, and are discussed in Item VI.)

D2 describes a particle analyser for sensing particles carried in a sheath fluid flowing past a detector, in which each particle is illuminated by a slit-shaped beam and viewed by a similarly shaped detector, comprising a linear array of photodiode sensors (see

col. 6, line 62). A flow cell 16 is used to pass the sample through the light beam.

D3 discloses a flow cytometer for counting particles flowing in a sheath fluid, in which the detector is a photomultiplier, detecting the presence of particles as they pass, rather than investigating an image of a particle or particles.

D4 relates to measuring geometric properties of a particle in a fluid, which may be moving, in which a CCD camera is used to investigate an speckle pattern image of the particle. Particle shape may be investigated. No details of the sample container are disclosed.

D6 relates to a particle analyser, in which particles in a sheath fluid flow through a flow cell 100.This includes a measurement portion 152, where the sample passes between two flat parallel walls, so that an image of a plurality of particles simultaneously can be detected by a TV camera 5 (see e.g. col.6, lines 31-37).

D7 relates to an apparently disposable cartridge, with rupturable parts, for mixing a sample with diluents, there being a measurement chamber 140 part for light transmission investigation.

D8 relates to a particle analyser in which a sheathed sample is passed through an optical flow cell, which has an extended imaging area 18 such that a number of particles can be imaged on a CCD camera simultaneously.

D9 describes a sheathed flow particle analyser, again with imaging onto a CCD camera 83.

D10 describes a particle analyser in which a flowing sample passes through a flat sheath flow cell, the particles being imaged on a line sensor.

D11 discloses a sampling device ,(Fig. 8) comprising a syringe into which the sample is there being a measuring chamber formed by windows 47a, 47b, a filter 48 preventing exit of the sample.

D12 - D15 each disclose an example of a sample cell, for optical tests, having differing

cross sectional zones along its length, an exposing area, and "no sample outlet". D14 and D15 refer to the use of reagents on or in parts of the device.

3. Novelty and inventive step:

Claims 1 and 59:
(These are of substantially corresponding scope, and will be dealt with together).
It is well known in a flow system to spread out the sample over an area so as to measure and analyse a plurality of particles simultaneously - see e.g. D6, D8, D10. This involves complicated synchronisation techniques to capture the images before analysis thereof.
The use of such a particle analysing system on a still sample, e.g. contained in a sample container as in D7, D11, D12, D13, D14, D15 would be simpler, and would be obvious to the skilled person in this field.
Also it would be obvious to adapt the flat flow cells to enable still sample tests, and avoid the need for an outlet.
Thus the subject matter of claims 1 and 59 does not involve an inventive step.

Claim 97:
(This claim is obscure in scope since it is not clear to what degree the passages concerning the detector or the means for arranging, restrict the scope thereof).
As far as can be seen, the subject matter actually defined is anticipated by a simple test tube with part of its internal surface coated or applied with reagent. A test tube has an inlet, a part of its length which could be considered to act as a flow passage or system, and a part at the bottom which can be considered as the sample compartment. More sophisticated test tubes, cuvettes, which have different cross sectional parts, and complex disposable analysis cartridges, would read on even more clearly - see e.g. D14, D15. It would seem that there are many more examples available in the art.

It would be obvious from the teaching of D14 or D15 to apply reagent to part of the containers of D7, D11 (fig.8), D12, or D13. The flat areas of these containers would permit viewing by a detector so as to allow some sort of imaging.
Thus claim 97 is not novel from D14, D15, and not inventive from the combinations referred to above.

Dependent claims 2-58, 60-96, 98-129:
The dependent claims seem to relate to mere design modifications, consequential features of the basic system of claims 1,59 and 97, or conventional features, and thus do not add anything inventive to these claims.

Re Item VI
Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
D1.....WO9850777	12.11.98	05.05.98	05.05.97 09.12.97
D5.....EP-A-0950890	20.10.99	13.04.99	13.04.98

D1 anticipates claim 1: devices with sample compartments are shown in figs. 6,7. The valve 607 does not allow the sample to exit (see page 34 first paragraph). Clearly a sample is introduced, the device is arranged in relation to a detection device - see measurement apparatus of fig. 8, description pages 38,39 etc. As described on page 40 or 42, a CCD camera is used to form a spatial image of the sample domain.
D1 likewise anticipates the device claim 59.
Claim 97 is also anticipated by D1, see also references to a closable valve 607 and reagent container 604, on page 33, line 27 to page 34, line 7.
In view of the fact that the devices used in D1 are identical to those shown in the figures of the present application, it would appear that many of the dependent claims are anticipated by D1.

D5 describes a sheath flow system for particle image analysis.

Re Item VII
Certain d fects in the international application

Prior art documents (other than D1 and D5) should have been referred to in the description.

Re Item VIII
Certain observations on the international application

1. The presence of a plurality of independent claims (59,97) of varying scope and including features repeated using only slightly varying terminology results in a general lack of conciseness in the claims. It should be noted that claim 1 does not refer to the reagent. As far as can be seen, the device claim could have been claim 1, and the system could have referred to a system, with the reference to the device therein, referring to the device being as claimed in claim 1. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.

2. Clarity and support in the description:
a. Claims 1,59, and 97 are generally obscure in scope and not clearly supported by the description.
b. The feature which has been added to these claims by amendment: "without a sample outlet" and "no sample outlet", is based on page 7, lines 11-13, but does not correspond clearly with the described embodiments. The described devices, such as that of figure 1, have a sample outlet from the exposing area or sample compartment 106, leading to a valve. It is admitted that here there can be the facility that the valve closes on contact with the sample (see page 25, line 7), but this does not clearly read onto the amended feature.
(Note: The amendment in claims 1, 58 and 97 concerning "no sample outlet", is said to be based on page 7, lines 11-13, but this passage referred only to some embodiments, and it is not clear how it applies thereto. It would appear that there may have been an extension beyond the original disclosure here, since claims or definitions of the present breadth were never clearly disclosed in the original application. This objection has not however been raised formally in Item I).
The claim should have been amended to more clearly define the constructions envisaged.

c. It should also be noted that the original claims gave the impression that the device and the method related to analysis in which the sample was flowing through the device. The references to flow and flow system have still been retained in the present claims, which seem to be in contradiction to the idea of the sample being introduced and not being able to exit the device. The change in scope of the claims has led to the need to cite further prior art documents, those cited apparently being only examples.

d. In claim 97 there appears to be no clear restrictive effect in the matter at lines 3-7, relating to the function of the exposing domain.

e. In claims 58, and 97, the nature of "means for arranging", and in claim 1, the step of "arranging...." are not clear.

f. In claim 1, the meaning of "spatial image data" is not clear.

Claims

1. A method for the assessment of at least one parameter of particles in a liquid analyte material, comprising

providing a device comprising a sample compartment comprising an exposing domain, an inlet through which a volume of a liquid sample representing the analyte material can been introduced, and a flow system comprising at least a channel allowing at least a portion of the volume of the liquid sample to flow within the device, the device being without a sample outlet,

introducing a volume of the liquid sample in the device through the inlet of the device, passing at least a portion of the volume of the liquid sample through the flow system of device the into the exposing domain of the sample compartment,

arranging the device in relation to detection device comprising detection means for quantitatively detecting spatial image data and processing means for processing the detected image presentation

detecting electromagnetic signals from the sample in the exposing domain of th device in the detection device forming, in the detection device, a spatial image representation of the exposing domain, and

processing the detected image presentation obtaining the assessment of the at least one parameter.

2. A method according to claim 1, whereby the device comprising the sample compartment is disposable.

3. A method according to claim 1, wherein one or more reaction components initially loaded in a compartment or flow channel part of the flow system of the disposable device is added to at least a portion of the volume of the liquid sample representing the analyte material.

4. A method according to claim 3, wherein the reaction components comprise one or more chemicals.

5. A method according to claim 3 or 4, wherein at least one of the reaction components initially loaded in the compartment or flow channel part is in solid form.

6. A method according to claim 5, wherein the reaction components comprise one or more chemicals in solid form in combination with one or more solubilizing agents aiding the solubilization of the chemicals in the liquid sample.

AMENDED SHEET

7. A method according to claim 5 or 6, wherein at least one of the reaction components has been loaded in freeze-dried form.

8. A method according to any of claims 2-7, wherein the amounts and availability of the reaction components and the design of the flow system are so adapted that a predetermined minimum of the reaction components will be contained in the liquid sampl present in the sample compartment.

9. A method according to claim any of claims 2-8, wherein any longitudinal gradient present in the liquid sample in the flow system is substantially reduced by passing the liquid sample through a part of a flow channel of the flow system of the device having a shape and/or size resulting in substantially reduction of longitudinal gradients in liquids passing therethrough.

10. A method according to claim 9, wherein the part of the flow channel is a flow channel providing substantial laminar flow therethrough.

11. A method according to any of claims 2-8, wherein any radial gradient present in the liquid sample in the flow system is substantially reduced by passing the liquid sampl through a part of a flow channel of the flow system of the device having a shape and/or size resulting in substantially reduction of radial gradients in liquids passing therethrough.

12. A method according to claim 11, wherein the part of the flow channel has at least one bend or obstruction resulting in substantially turbulent flow in the liquid passing th bend or obstruction

13. A method according to any of the preceding claims, wherein the flow of the liquid sample in the device is provided by a propelling means provided in the device.

14. A method according to claim 13, wherein the propelling means is provided in an adapter device with which the device is engaged during liquid sample acquisition.

15. A method according to claim 13, wherein the propelling means constitutes an integrated part of the device.

16. A method according to any of the preceding claims, wherein the velocity of the flow into, within, or out of the device is regulated by means of one or more regulating means constituting part of the flow system.

17. A method according to claim 16, wherein the velocity regulating means comprise means selected from stop valves, one way valves, and pressure and/or speed reduction valves.

AMENDED SHEET

18. A method according to any of the preceding claims, wherein one or more operations selected from the group consisting of filtration, concentration and magnetic attraction is/are performed, the device comprising the means for performing such operation or operations.

19. A method according to any of the preceding claims, wherein the device and its operation and the operation of the combination of the detecting device or devices with the device engaged therewith are adapted so that the sample contained in the exposing domain permits a reproducible determination or assessment of the parameter or parameters to be determined or assessed.

20. A method according to claim 19, wherein the parameters of the sample in the exposing domain permit the formation of a spatial image presentation the background of which is within the operational dynamic limits of the detection device, and the sample is in substantial spatial equilibrium throughout the volume of the exposing domain during the detection.

21. A method according to claim 19, wherein the parameters of the sample in the exposing domain permit the formation of a spatial image presentation the background of which is within the operational dynamic limits of the detection device, and the sample in the exposing domain is not in substantial equilibrium throughout the volume of the exposing domain during the detection, the detection and the processing of the image data substantially securing distinction between particles and background.

22. A method according to any of the preceding claims, wherein any dimensions of the device which influence the volume of sample represented in the spatial image representation are kept within predetermined variations from device to device.

23. A method according to any of claims 1-21, wherein variations, between individual devices, in dimensions which influence the volume of sample represented in the spatial image representation, are indicated on the devices in that each device is associated with information as to data concerning the dimensions in question, and the information is taken into consideration in the processing of the detected image presentation.

24. A method according to claim 23, wherein the information as to data concerning the dimensions in question is contained in insignia carried by the devices and readable by the detection device or another device adapted to read the insignia.

25. A method according to claim 24, wherein the data concerning the dimensions in question are transferred to the processing means of the d tection device to enable the

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processing means to take the data into consid ration in the processing of the detected image pres ntation.

26. A method according to claim 25, wherein the transfer of the data to the processing means is performed automatically or through human interaction.

27. A method according to claim 26, wherein automatic transfer of data concerning th dimensions is only performed when an authentication insignia has been identified.

28. A method according to claim 27, wherein the authentication insignia is an image or other insignia proprietary to a producer or distributor of the devices authorised by a private or official body to provide the devices for the determination or assessment in question.

29. A method according to claim 27, wherein the authentication insignia comprise of encrypted information or a trademark, and the detection device or other device is capable of decrypting the encrypted information or identifying the trademark.

30. A method according to any of claims 1-21, wherein variations in dimensions of the device which influence the volume of sample represented in the spatial image representation are compensated in the assessment on the basis of volume calibration means.

31. A method according to claim 30, wherein the volume calibration means is constituted by one or more of the reaction components, in which case the reaction component or components in question is/are loaded in a predetermined concentration, and the flow operation of the device is performed in a manner ensuring that the predetermined concentration will be reflected in the concentration of the reaction component or components in the exposing domain.

32. A method according to any of claims 1-30, wherein one or more reaction components and/or diluents have been added to the sample, and the proportion of the volume of sample in the exposing domain which corresponds to the original sample representing the analyte material is assessed by detecting and processing one or more signals substantially originating from the one or more reaction components and/or diluents added.

33. A method according to any of the preceding claims, wherein the detection of the spatial image representation is performed by means of an array of active detection elements onto which array the spatial image presentation is exposed.

34. A method according to claim 33, wherein intensities detected by the array of detection elements are processed in such a manner that representations of

electromagnetic signals from the particles are identified as distinct from representations of electromagnetic background signals.

35. A method according to claim 34, wherein the size of the volume of the liquid sample is sufficiently large to permit the assessment of the at least one quantity parameter or the at least one quality parameter to fulfil a predetermined requirement to the statistical quality of the assessment based on substantially one exposure.

36. A method according to any of the preceding claims, wherein the signal which is detected by detection device is a signal which is substantially caused by attenuation of electromagnetic signal, and/or by emission of electromagnetic irradiation by photoluminescence, the attenuation and/or the photoluminescence being associated to one or more molecules which is/are a part of the particle, preferably where the particle is somatic cell or bacteria, and where the molecules are DNA and/or proteins.

37. A method according to any of the preceding claims, wherein the signal which is detected by detection device substantially originates from one or several types of molecules of types which bind to, are retained within, or interact with, the particles, such molecules being added to the sample before or during exposure of electromagnetic signals, the molecules being molecules giving rise to one or several of the following phenomena: attenuation of electromagnetic radiation, photoluminescence when illuminated with electromagnetic radiation, scatter of electromagnetic radiation, raman scatter.

38. A method according to any of the preceding claims, one or more reaction components initially loaded in a compartment or flow channel part of the flow system of the device is one or more nucleic acid dyes and/or one or more potentiometric membrane dyes.

39. A method according to claim 38, wherein a nucleic acid dye or nucleic acid dyes is/are added in an amount of 0.3-30 µg per ml of the sample.

40. A method according to claim 38 or 39, wherein one or more nucleic acid dyes is/are selected from the group consisting of: phenanthridines (e.g. ethidium bromide CAS#: 1239-45-8, propidium iodide CAS#: 25535-16-4), acridine dyes (e.g. acridine orange CAS#: 65-61-2/CAS#: 10127-02-3), cyanine dyes (e.g. TOTO™-1 iodide CAS#: 143 413-84-7 -Molecular Probes, YO-PRO™-1 iodide CAS#: 152 068-09-2 -Molecular Probes), indoles and imidazoles (e.g. Hoechst 33258 CAS#: 023 491-45-4, Hoechst 33342 CAS#: 023 491-52-3, DAPI CAS#: 28718-90-3, DIPI (4',6-(diimidazolin-2-yl)-2-phenylindol)).

41. A method according to claim 38 or 39, wherein the nucleic acid dye added is propidium iodide CAS#: 25535-16-4.

42. A method according to any of claims 37-41, wherein any reaction component added has the effect of aiding in the binding of one or more dyes to a particle, pr ferably such chemical being t-Octylphenoxypolyethoxyethanol (Triton X-100).

43. A method according to any of the preceding claims, wherein any reaction component has the effect of increasing the rate of dissolution or solubilisation of any chemical on a substantially solid, and/or substantially non-aqueous, and/or substantially freeze dried form, preferably such chemical being one or more types of organic or inorganic salts.

44. A method according to any of the preceding claims, wherein particle being assessed is a result of one or several reaction(s) between one or more antibodies and one or more antigens.

45. A method according to any of the preceding claims, wherein particle being assessed is a particle being and/or containing one or more specific protein(s)

46. A method according to any of the preceding claims, wherein the assessment of particles is carried out substantially simultaneously with the determination of the amount and/or the level of any constituent in said sample material, the constituent being determined being, e.g., one or several of: fat, protein, lactose, urea, citric acid, glucose, ketones, carbon dioxide, oxygen, pH, potassium, calcium, sodium.

47. A method according to claim 46, wherein the determination of any chemical property is based on spectrophotometric measurement, the spectrophotometric measurement being, e.g., one or several of; mid-infrared attenuation, near-infrared attenuation, visible attenuation, ultra-violet attenuation, photoluminescence, raman scatter, nuclear magnetic resonance.

48. A method according to claim 46 or 47, wherein the determination of any chemical property is based on potentiometric measurement, preferably by the use of ion selective electrode.

49. A method according to any of the preceding claims, wherein the interior of the sample compartment has an average thickness of between 20 µm and 2000 µm.

50. A method according to claim 49, wherein the interior of the sample compartment has an average thickness of between 20 µm and 1000 µm.

51. A method according to claim 50, wherein the interior of the sampl compartment has an average thickness of between 20 µm and 200 µm.

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52. A method according to any of the preceding claims, wherein sample compartment has dimensions, in a direction substantially parallel to an exposing window, in the range between 1 mm by 1 mm and 10 mm by 10 mm.

53. A method according to any of the preceding claims, wherein the volume of the liquid sample from which electromagnetic radiation is exposed, is in the range between 0.01 µl and 20 µl.

54. A method according to claim 53, wherein the volume of the liquid sample from which electromagnetic radiation is exposed, is in the range between 0.04 µl and 4 µl.

55. A method according to any of the preceding claims, wherein detection of signal from exposing domain, where at least one physical dimension of the domain substantially partly determines the volume of the domain, and where the at least one physical dimension is substantially different during at least a part of any period when a sample is introduced to the domain and at least a part of any period when detection is performed, preferably where the effect is such that the volume of the domain is substantially larger during at least a part of any period when a sample is introduced to the domain than in at least a part of any period when detection is performed.

56. A method according to claim 55, wherein the volume during at least a part of any period when a sample is introduced to the domain is at least 10% larger than the volume during at least a part of any period when detection is performed, preferably where the volume is 25% larger, more preferably where the volume is 50% larger, more preferably where the volume is 100% larger, more preferably where the volume is 200% larger, more preferably where the volume is 400% larger.

57. A method according to claim 55 or 56, wherein the effect of the changes of the at least one physical dimension, is the at least substantial replacement of part of a sample in the domain with a different part of the sample, allowing detection of signals from substantially different part of the sample.

58. A method according to any of the preceding claims, wherein detection of signal by detection device, used for the determination or assessment of at least one quantity parameter and/or at least one quality parameter of particles, is initiated and/or controlled by the introduction of a device into an instrument containing the detection device.

59. A system for the asessment of at least one parameter of particles in a liquid analyte material, comprising

a device comprising a sample compartment comprising an exposing domain, an inlet through which a volume of a liquid sample representing the analyte material can

been introduced, and a flow system comprising at least a channel allowing at least a portion of the volume of the liquid sample to flow within the device, the device being without a sample outlet,

a detection device comprising detection means for quantitatively detecting spatial image data and processing means for processing the detected image presentation,

the device and the detection device having means for arranging the device in relation to the detection device in a manner allowing electromagnetic signals from a sampl in the exposing domain of the device to pass to the detection device and to form, in the detection device, a spatial image representation of the exposing domain.

60. A system according to claim 59, wherein the flow system additionally comprises a compartment or a flow channel part in or from which at least part of one or more reaction components initially loaded in the compartment or flow channel part is added to at least a portion of the volume of the liquid sample representing the analyte material.

61. A system according to claim 60, wherein the reaction components comprise one or more chemicals.

62. A system according to claim 60 or 61, wherein at least one of the reaction components loaded in the compartment or flow channel part is in solid form.

63. A system according to claim 62, wherein the reaction components comprise one or more chemicals in solid form in combination with one or more solubilizing agents aiding the solubilization of the chemicals in the liquid sample.

64. A system according to claim 61 or 62, wherein at least one of the reaction components is in freeze-dried form.

65. A system according to any of claims 59-64, wherein at least a part of a flow channel of the flow system of the device has such a shape and/or size that passage of the liquid sample through it will substantially reduce any longitudinal gradient present in the liquid sample.

66. A system according to claim 65, wherein the part of the flow channel provides substantial laminar flow therethrough and/or comprises one or more mixing chambers.

67. A system according to any of claims 59-66, wherein at least a part of a flow channel of the device has such a shape and/or size that passage of the liquid sample through it will substantially reduce any radial gradient pres nt in the liquid sample.

68. A system according to claim 67, wh rein the part of the flow channel has at least one bend or obstruction resulting in substantially turbulent flow in liquid passing the bend or obstruction.

69. A system according to any of claims 59-68, wherein the flow of the liquid sample in the device is provided by a propelling means provided in the device or in a device with which the device can be engaged.

70. A system according to claim 69, wherein the propelling means is provided in an adapter device with which the device is engaged during liquid sample acquisition.

71. A system according to claim 69, wherein the propelling means constitutes an integrated part of the device.

72. A system according to any of claims 59-71, wherein the flow system comprises one or more means for regulating the velocity of the flow into, within, or out of the device.

73. A system according to claim 72, wherein the velocity regulating means comprise means selected from stop valves, one way valves, and pressure and/or speed reduction valves.

74. A system according to any of claims 59-73, wherein the device comprises means for performing one or more operations on the liquid sample, the operations being selected from the group consisting of filtration, concentration and magnetic attraction.

75. A system according to any of claims 59-74, wherein the device and its operation and the operation of the combination of the detecting device or devices with the devic engaged therewith are adapted so that the sample contained in the exposing domain permits a reproducible determination or assessment of the parameter or parameters to be determined or assessed.

76. A system according to any of claims 59-75, wherein any dimensions of the device which influence the volume of sample represented in the spatial image representation are kept within predetermined variations from device to device.

77. A system according to any of claims 59-75, wherein variations, between individual devices, in dimensions which influence the volume of sample represented in the spatial image representation, are indicated on the devices in that each device is associated with information as to data concerning the dimensions in question, and the information is taken into consideration in the processing of th detected image presentation.

78. A system according to claim 77, wherein the information as to data concerning the dimensions in question is contained in insignia carried by the devices and readable by the detection device or another device adapted to read th insignia.

79. A system according to claim 78, wherein the reading of the insignia by the detection device or another device and/or the inclusion of the information as to data concerning the dimensions in the processing of the detected image presentation is only performed when the detection device contains an authentication insignia.

80. A system according to claim 79, wherein the authentication insignia is an image or other insignia proprietary to a producer or distributor of the devices authorised by a private or official body to provide the devices for the determination or assessment in question.

81. A system according to claim 79, wherein the authentication insignia comprise of encrypted information or a trademark, and the detection device or other device is capable of decrypting the encrypted information or identifying the trademark and to take the dimension information into consideration only upon successful decryption or identification.

82. A system according to any of claims 59-75, wherein variations in dimensions of the device which influence the volume of sample represented in the spatial imag representation are compensated in the assessment on the basis of volume calibration means.

83. A system according to claim 82, wherein the volume calibration means is constituted by one or more of the reaction components, in which case the reaction component or components in question is/are loaded in a predetermined concentration, and the device is capable of providing a flow operation ensuring that the predetermined concentration will be reflected in the concentration of the reaction component or components in the exposing domain.

84. A system according to any of claims 59-83, wherein the signal which is detected by detection device is a signal which is substantially caused by attenuation of electromagnetic signal, and/or by emission of electromagnetic irradiation by photoluminescence, the attenuation and/or the photoluminescence being associated to one or more molecules which is/are a part of the particle, preferably where the particle is somatic cell or bacteria, and where the molecules are DNA and/or proteins.

85. A system according to any of claims 59-84, one or more reaction components initially loaded in a compartment or flow channel part of the flow system of the device is one or more nucleic acid dyes and/or one or more potentiometric membrane dyes.

86. A system according to claim 85, wherein a nucleic acid dye or nucleic acid dyes is/are added in an amount of 0.3-30 µg per ml of the sample.

87. A system according to any of claims 59-86, wherein any reaction component has the effect of increasing the rate of dissolution or solubilisation of any chemical on a substantially solid, and/or substantially non-aqueous, and/or substantially freeze dried form, preferably such chemical being one or more types of organic or inorganic salts.

88. A system according to any of claims 59-87, wherein the determination of a chemical property of the sample is based on spectrophotometric measurement, the spectrophotometric measurement being, e.g., one or several of; mid-infrared attenuation, near-infrared attenuation, visible attenuation, ultra-violet attenuation, photoluminescence, raman scatter, nuclear magnetic resonance.

89. A system according to claim 88, wherein the determination of any chemical property is based on potentiometric measurement, preferably by the use of ion selective electrode.

90. A system according to any of claims 59-89, wherein the interior of the sample compartment has an average thickness of between 20 µm and 2000 µm.

91. A system according to claim 90, wherein the interior of the sample compartment has an average thickness of between 20 µm and 1000 µm.

92. A system according to claim 91, wherein the interior of the sample compartment has an average thickness of between 20 µm and 200 µm.

93. A system according to any of claims 59-92, wherein sample compartment has dimensions, in a direction substantially parallel to an exposing window, in the range between 1 mm by 1 mm and 10 mm by 10 mm.

94. A system according to any of claims 59-93, wherein the volume of the liquid sample from which electromagnetic radiation is exposed, is in the range between 0.01 µl and 20 µl.

95. A system according to claim 94, wherein the volume of the liquid sample from which electromagnetic radiation is exposed, is in the range between 0.04 µl and 4 µl.

96. A system according to any of claims 59-95, wherein detection of signal by detection device, used for the determination or assessment of at least one quantity parameter and/or at least one quality parameter of particles, is initiated and/or controlled by the introduction of a device into an instrument containing the detection device.

97. A device adapted to be used in a system for the assessment of at least one parameter of particles in a liquid analyte material, the device comprising

a sample compartment comprising an exposing domain allowing electromagnetic signals from a sample in the exposing domain of the device to pass to a detection device and to form, in the detection device, a spatial image representation of the exposing domain processable by processing means of the detection device,

an inlet through which a volume of a liquid sample representing the analyte material can been introduced and no sample outlet,

a flow system comprising at least a channel allowing at least a portion of the volume of the liquid sample to flow within the a device, and

means for arranging the a device in relation to the detection device,

wherein the flow system additionally comprises a compartment or a flow channel part in or from which at least part of one or more reaction components initially loaded in the compartment or flow channel part is added to at least a portion of the volume of the liquid sample representing the analyte material.

98. A device according to claim 97, wherein the reaction components comprise one or more chemicals.

99. A device according to claim 97 or 98, wherein at least one of the reaction components loaded in the compartment or flow channel part is in solid form.

100. A device according to claim 99, wherein the reaction components comprise one or more chemicals in solid form in combination with one or more solubilizing agents aiding the solubilization of the chemicals in the liquid sample.

101. A device according to claim 99 or 100, wherein at least one of the reaction components is in freeze-dried form.

102. A device according to any of claims 97-101, wherein the amounts and availability (solubility and/or dispersibility under the conditions prevailing) of the reaction components and the design of the flow system are so adapted that a predetermined minimum of the reaction components will be contained in the liquid sample present in the sample compartment.

103. A device according to any of claims 97-102, wherein at least a part of a flow channel of the flow system of the device has such a shape and/or size that passage of the liquid sample through it will substantially reduce any longitudinal gradient present in the liquid sample.

104. A device according to claim 103, wherein the part of the flow channel provides substantial laminar flow therethrough and/or comprises one or more mixing chambers.

105. A device according to any of claims 97-104, wherein at least a part of a flow channel of the device has such a shape and/or size that passage of the liquid sample through it will substantially reduce any radial gradient present in the liquid sample.

106. A device according to claim 105, wherein the part of the flow channel has at least one bend or obstruction resulting in substantially turbulent flow in liquid passing the bend or obstruction.

107. A device according to any of claims 97-106, wherein the flow of the liquid sample in the device is provided by a propelling means provided in the device or in a device with which the device can be engaged.

108. A device according to claim 107, wherein the propelling means is provided in an adapter device with which the device is engaged during liquid sample acquisition.

109. A device according to claim 107, wherein the propelling means constitutes an integrated part of the device.

110. A device according to any of claims 97-109, wherein the flow system comprises one or more means for regulating the velocity of the flow into, within, or out of the device.

111. A device according to claim 110, wherein the velocity regulating means comprise means selected from stop valves, one way valves, and pressure and/or speed reduction valves.

112. A device according to any of claims 97-111, which device comprises means for performing one or more operations on the liquid sample, the operations being selected from the group consisting of filtration, concentration and magnetic attraction.

113. A device according to any of claims 97-112, wherein any dimensions thereof which influence the volume of sample represented in the spatial image representation are kept within predetermined variations from device to device.

114. A device according to any of claims 97-113, which carries information relating to data concerning dimensions of the device which influence the volume of sample represented in the spatial image representation.

115. A device according to claim 114, wherein the information as to data concerning the dimensions in question is contained in insignia carried by the device and readable by the detection device or another device adapted to read the insignia.

116. A device according to any of claims 97-115, wherein variations in dimensions of the device which influence the volume of sample represented in the spatial image representation are compensated in the assessment on the basis of volume calibration means.

117. A device according to any of claims 97-116, where one or more reaction components initially loaded in a compartment or flow channel part of the flow system of the device is one or more nucleic acid dyes and/or one or more potentiometric membrane dyes.

118. A device according to any of claims 97-117, containing one or more compartment(s) or domain which allow on spectrophotometric measurement for the determination of any chemical property, the spectrophotometric measurement being, e.g., one or several of; mid-infrared attenuation, near-infrared attenuation, visible attenuation, ultra-violet attenuation, photoluminescence, raman scatter, nuclear magnetic resonance.

119. A device according to claim 118, containing one or several ion selective electrodes for the determination of any chemical property is based on potentiometric measurement.

120. A device according to any of claims 97-119, wherein the interior of the sample compartment has an average thickness of between 20 µm and 2000 µm.

121. A device according to claim 120, wherein the interior of the sample compartment has an average thickness of between 20 µm and 1000 µm.

122. A device according to claim 121, wherein the interior of the sample compartment has an average thickness of between 20 µm and 200 µm.

123. A device according to any of claims 97-122, wherein sample compartment has dimensions, in a direction substantially parallel to an exposing window, in the range between 1 mm by 1 mm and 10 mm by 10 mm.

124. A device according to any of claims 97-123, wherein the volume of the sample compartment from which electromagnetic radiation is exposed, is in the range between 0.01 µl and 20 µl.

125. A device according to claim 124, wherein the volume of the sample compartment from which electromagnetic radiation is exposed, is in the range between 0.04 µl and 4 µl.

126. A device according to any of claims 97-125, wherein detection of signal from exposing domain, where at least one physical dimension of the domain substantially partly determines the volume of the domain, and where the at least one physical dimension is substantially different during at least a part of any period when a sample is introduced to the domain and at least a part of any period when detection is performed, preferably where the effect is such that the volume of the domain is substantially larger during at least a part of any period when a sample is introduced to the domain than in at least a part of any period when detection is performed.

127. A device according to claim 126, wherein the volume during at least a part of any period when a sample is introduced to the domain is at least 10% larger than the volume during at least a part of any period when detection is performed, preferably where the volume is 25% larger, more preferably where the volume is 50% larger, more preferably where the volume is 100% larger, more preferably where the volume is 200% larger, more preferably where the volume is 400% larger.

128. A device according to claim 126 or 127, wherein the effect of the changes of the at least one physical dimension, is the at least substantial replacement of part of a sample in the domain with a different part of the sample, allowing detection of signals from substantially different part of the sample.

129. A device according to claim 97, wherein the a device comprises means for disengaging the device from the detection device after the detection by the detection means.